HEPATIC AND RENAL IMPAIRMENT IN ANTICOAGULANT RODENTICIDE POISONING

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Abstract

This paper aims to highlight the impairment of the renal and hepatic function in anticoagulant rodenticide poisonings. The study involves 40 cases taken from the archive of the Veterinary Emergency Hospital within the Faculty of Veterinary Medicine in Cluj-Napoca between 2017 - 2022, 7 cats and 33 dogs.

This article collects important laboratory values, we elaborated a database to be able to diagnose, treat and evaluate the renal and hepatic status of these animals. For the hematology part a VetScan HM5 device was used, thrombocytopenia was found, the erythrocytes, haemoglobin and haematocrit had lower values. For the biochemistry part we used a PrimeVet device, we detected important changes in the level of glucose, lactate, total bilirubin, smaller changes in creatinine and urea. For the coagulation tests a Quickvet specialty analyser was used, the prothrombin time in 50% of the cases presented low values, 14% presented normal values, and in 36% had high values. In each case the partial thromboplastin activation time presented high values. We detected kidney insufficiency in 2 cats and 3 dogs, and liver problems in 2 cats and 8 dogs.

Key words: rodenticide, coagulation, haematology.

INTRODUCTION

The intoxications with first generation or second generation anticoagulant rodenticides in pets are frequently seen (Valchev et al., 2008).

The main purpose of this research is to highlight the liver disfunctions and kidney damage in case of poisonings with anticoagulant rodenticides and to establish the percentage of patients who developed liver or kidney disfunction or suffer from both at the same time.

Rodenticide anticoagulants from the first and second generation are the most used to combat rodents, these substances will affect the blood clotting processes, leading to death by internal or external haemorrhages (Gunja et al., 2011; Subban et al., 2012). The intoxicated animals will constantly lose blood in small amounts, remain conscious until death accrues. accompanied by severe pain. Although it is not known exactly how long it may take for an animal to die, as this period is highly influenced by the dose ingested by the animal and its body weight, some studies have concluded that this time is about 3 days for rats, others describe a week, and in case of mice it may last a little bit longer (Berny et al., 1995; Munday and Thompson, 2003; Wu et al. 2012; Casner, 1998; Baker et al., 2002).

These anticoagulants are also dangerous to non-targeted animals, such as wild animals and companion animals, these can consume the baits for rodents, or the poisoned animal itself. The first generation anticoagulants persists for about 7 days in an animal's organism, but

second generation anticoagulants are much stronger, persisting for about 4 weeks in the body. The mechanism of action of all anticoagulant rodenticides is through inhibition of vitamin K₁ epoxide reductase (Breckenridge et al., 1985), this will lead to coagulopathy, due to the reduction of the active forms of coagulation factors: II, VII, IX and X (Craciun, 1998). Because these factors are active in fibrin formation, they need to be able to bond calcium, which is possible if each coagulation factor present in their structure carboxylic acid. Vitamin K_1 intervenes on the coagulation factors by adding the second carboxylic acid. produce a post-translational modification of the coagulation factor protein and becomes a vitamin K₁-epoxide oxidase, during this process. Vitamin K₁ epoxide can normally be returned to its original vitamin K₁, with the help of enzymes, being a recycling of vitamin K1.

At this stage rodenticide anticoagulants will inhibit the activity of these enzymes, resulting a decrease in the amount of vitamin K_1 and an increase in the concentration of vitamin K_1 epoxide in the hepatocytes and in the plasma. After the almost complete depletion of these factors and vitamin K_1 , clinical coagulopathy occurs (Walker et al., 2012). This time interval explains the delay in the appearance of clinical signs, which can reach up to 5 days after the ingestion of anticoagulant rodenticides and can be correlated with haematological, biochemical laboratory analyses and coagulation times.

MATERIALS AND METHODS

The study involved 40 cases taken from the archive of the Emergency Veterinary Hospital of the Faculty of Veterinary Medicine in Cluj-Napoca, over a period of 5 years, between 2017 and 2022, and included 7 cats and 33 dogs.

The cats ranged in age from 3 months to 9 years, 5 of them were male and 2 females. The dogs were aged between 3 months and 11.5 years, 16 cases are male and the remaining 17 are female. Among the dogs, we had: 10 Mestizos, 4 Labradors, 3 Bichons, 2 Beagles, 2 Huskies, 3 German shepherds, a Dachshund, a Mioritic shepherd, a French bulldog, a Pincher, a Tosa inu, an Akita inu, a Hungerian vizsla, a Dalmatian, and a Golden retriever.

RESULTS AND DISCUSSIONS

In order to obtain a complete panel about this poisoning and to facilitate the work of clinicians, to make quick and correct diagnoses and efficient treatments, the data's obtained were processed statistically, and will be presented in tables, in 3 categories. We will present the general clinical signs, haematology values, biochemical data's and coagulogramma results.

Cats show mild to moderate bradycardia, with mild to severe tachypnea and the body temperature was in 33.33% low, 33.33% normal and high in 33.33% cases. The data is being arranged in Table 1.

Nr caz	Nr crt	Age	Sex	CRT (Sec)	Mucous membr.	FC.	FR.	Temp (°C)
4	1	9 years	М	1	Pale pink	116↓	4 0 ↑	36,4↓
7	2	4 years	м	-	Pale pink	-	-	39,13
13	3	3 month	м	2	Pale pink	100↓	30 ↑	37,0↓
23	4	l year	М	-	-	-	-	-
31	5	6 month	м	3	Pale pink	136 ↓	112↑	39,9↑
39	6	6 month	F	3	Pale pink	-	-	40,9 ↑
40	7	6 month	F	2	Pale pink	-	160↑	38,2

In the haematology part (Table 2), the changes were not so obvious, regarding the haematocrit and the red blood cell volume, these values tend to decrease.

Table 2. The haematology values in cats

Nr.	Nr.	WBC	RBC	HGB	HCT	MC	MCH	MCHC	PLT	MPV
case	Crt ·	10 º/L	10 ¹²	g/dL	%	V fL	рg	g/dL	10 %/L	£L
Ref		5,5-	5-10	8-15	24-45	39-	12,5-	30-36	300-	12-
Int.		19,5				55	17,5		800	17
4	1	7,93	9,28	11,8	28,2	30 ↓	12,7	41,6	164↓	7,1↓
7	2	5,5	6.29	8,2	28,43	45	13	28,8↓	35 ↓	9,6↓
13	3	-	-	11,4	38	-	-	-	-	-
23	4	-	-	12,45	40	-	-	-	-	-
31	5	-	-	15,1 ↑	4 6 ↑	-	-	-	-	-
39	6	-	-	8,6	27	-	-	-	-	
40	7	7,37	6,54	10,1	26,58	40,6	15,5	38,2 ↑	234↓	9,9↓

The increase of the MCHC can suggest a macrocytic anaemia, and in three pacients accured thrombocytopenia as similar changes were seen in other studies too (Kohn et al. 2003). Thrombocytopenia may also be caused

by vitamin K deficiency and decreased hepatic thrombopoietin synthesis (Andrew B., 2019).

Renal function impairment is seen in 2 cats out of 7 cases, these animals are presenting a high level of urea, this can also reflect a state of malnutrition, protein-deficient diet or liver disease. Glucose is irrelevant in felines, because they stress quickly which consequently will increase the glucose level too. Sodium and potassium show a slight increase in case 23, where the urea was increased too, these values reflecting a renal insufficiency. Total bilirubin can be elevated due to liver damage (Table 3). Most changes occur in the coagulogramm, where the prothrombin time and partial thromboplastin time are increased, due to the anticoagulant rodenticides interference with the vitamin K cycle.

Table 3. Biochemical datas in cats

Nr. caz	BUN mg/dL	Creat. mg/dL	Glu mg/dL	Na mmol/L	K mmol/L	Total bilirubina mg/dL	Acidul Lactic mmol/L
Ref	19-34	0,9-2,2	60-120	146-156	3,7-6,1	0,1-1,2	<2,5
4	19	1,4	136 个	155	3,9	0,7	1,1
7	-	1,2	101	-	-	-	-
13	9 🗸	0,6 ↓	102	146,5	4,88	2 个	1,8
23	126,5 ↑	-	111,75	158,5 个	6,27 个	-	1,65
31	38 个	1	138 个	154,4	4,17	0,7	11,1 个
39	15 🗸	0,7 ↓	146 个	150,8	4,29	2 个	1,3

Dogs presented pale mucous membranes to slight congested ones, possibly caused by hypovolemia, haemorrhage, shock or dehydration, some dogs had positive results at TFAST and AFAST, observing free fluid in the thorax and abdomen, due to internal bleeding. presented hematemesis or external haemorrhages as petechiae on the skin, vulva, and buccal cavity (Table 4).

All patients who exceeded the normal limits of respiratory rate presented tachycardia, that may

be due to cardiac causes, liver diseases, parasites or could appear because of a compensatory factor in hypovolemic states, shock, or excessive effort. As respiratory signs the animals presented dyspnoea, wet rales, emetic cough or coughs.

In dogs the haematology exam (Table 5) presented low values for erythrocytes that can be caused by haemorrhages, by damage to the kidney, especially affecting the secretion of erythropoietin. Hemoglobin and hematocrit decrease in anemic states, hemorrhages, liver and kidney diseases, etc. Elevated MCHC values indicate macrocystic anemia, and thrombocytopenia due to rodenticide poisoning. The urea level was elevated in 15.78% of the dogs, and in 10%, of the examinated animals we observed increased creatinine values to.

The glucose level was highly increased, but that could be related to the treatment.

The electrolytes were decreased, Na was presented lower levels in 35% of the dogs, K in 40% was decreased.

The total bilirubin in 47% of the cases was high, and the lactic acid was increased in 52.64% of the dogs (Table 6).

In anticoagulant rodenticide poisonings the coagulogramma results are the most trustful. In our research the results showed that the prothrombin time was in 50% from the examined animals decreased, normal in 14% and increased in 36% of the dogs (Figure 1). The partial thromboplastin activation time was in 100% elevated, the lowest value started from 20 sec and the highest measured maximum values was 200 sec. In a spontaneous intoxication with bromadiolone Binev et al., 2005 reported the prothrombin time was 122 s (reference range: 12-14 s) and the activated thromboplastin time was 88 s (reference range: 12-16 s).

Table 4. Clinical data in dogs

Nr	Age	Breed	Sex	CRT	Mucous	CF.	RF.	Temp.	Ā	т		Haemorrhages		Perista	Abdominal	Respiratory
case				(Sec)	Wendb.			(°C)	FAST	FAST	Int	Ext	Site	ltism	tenderness	disturbance
1	2 years	Half breed	F	2	congested	-	-	38,3	-	-	-	-	-	V	1	-
3	5 years	Bichon	F	2	pink	-	-	-	-	-	-	-	-	V	√	-
6	2 years	Labrador	F	3	congested	-	-	39,5 ↑	-	-	-		-	-	-	-
8	6 years	Half breed	F	1	congested	128	48 ↑	39,5↑	(-)	-	-	-	-	-	~	-
9	2 years	Half breed	F	-	pink	120	70 ↑	39,1	-	-	-	-	-	-	-	-
10	4 years	Labrador	F	-	pale pink	88	31	37,7 ↓	(-)	-	V	-	petechiae: lip and vulva		х	-
11	3 years	Mioritic	F	2	pale pink	-	-	38,3	-	-	-	-	-	-	-	-
12	3 years	BuldFran	М	2	pale	163 ↑	53 ↑	38,5	-	-	-	-	-	-	-	wet rales,cough
14	6 months	Half breed	м	5	pale	-	-	39,5↑		-	\checkmark	-	oral cavity	-	-	-
15	3 months	Beagle	М	3	pale pink	104 \downarrow	-	37,2	-	-	-	-	-	-	-	-
16	2 years	Half breed	F	1	pale pink	82 ↓	43 ↑	39	(+)	(+)	-	-	-	-	√.	whooping cough
17	8 years	Pinscher	F	-	-	-	-	38,6	-	-	V	-	hematemesis	V	\checkmark	reacted gastric mucosa
18	4 years	Half breed	М	2	pink	-	-	38,5	(-)	(-)	-	-	-	-	х	-
19	4 years	Tosa Inu	F	-	-	-	-	36,7 ↓	(-)	(+)			hemotorax	-	-	-
20	2 years	Husky	F	2	-	-	-	-	(-)	(-)	-	-	-	-	-	-
21	8 years	Husky	F	3	pale pink	-	-	38,7	-	-	-	-	-	-	-	-
22	2 years	Half breed	F	2	pale pink	120	24	40,6 ↑	(-)	-	-	V	Muco-haemorrhagic sialorrhea	-	-	-
24	5 months	Beagle	м	1	congested	110 \downarrow	56 ↑	38,9	-	-	-	V	oral cavity	-	-	-
25	5 years	Vizsla	М	-	pale pink	130	-	39,4 ↑	-	-	-	-	-	-	1	-
26	8 months	Half breed	м	2	pink	160 ↑	62 ↑	38	(-)	(+)	V	-	hemopericard	-	V	sever dispneea, pulmonary edemas
27	2 years	Dalmația	м	2	pale pink	130 ↑	40 ↑	39	(-)	(-)	-	-	-	-	1	-
28	1,5 years	Germ Shep	М	-	congested	-	-	40,9 ↑	-	-	-	-	-	-	-	slightly enlarged kidney
29	6 years	Bichon	F	1	pale pink	-	-	39,1	(-)	-	-	-	-	V	√	edematous gastric mucosa
32	8 years	Labrador	м	3	pale	120 ↑	70 ↑	38,2	(-)	(+)	V	-	hemotorax		V	whooping cough, pulmonary edema
34	2 years	Akita Inu	М	4	pale	110 ↑	30	39,8 ↑	-	-	-	-	-	-	-	-
35	3 months	Germ Shep	М	2	pink	-	-	38,5	-	-	-	-	-	-	-	-
36	3 years	Germ Shep	М	1	pale pink	104 ↑	28	39,1	-	-	-	-	-	-	-	-
37	11,5 years	Bichon	F	2	pink	128	$100\uparrow$	38,7	(-)	(-)	-	\checkmark	petechiae	-	-	-
38	6 years	Gold Retri	F	1	pale	120 ↑	116 ↑	39,9 ↑	-	(+)	-	-	-	-	-	dispneea

Table 5. Haematology in dogs

Nr.	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
case	10 ⁹ /L	1012	g/dL	%	£L	þà	g/dL	10 ⁹ /L
Norm	6-17	5 5 8 5	12-18	37-55	60-77	19 5-24 5	31-34	200-
	• • •	0,0 0,0	10 10	01 00		10,0 21,0	01 01	500
6	-	-	9.3 1	33 ⊥		-	-	
8	10,04	7.3	16,5	44.78	61	22,7	36,9 ↑	-
9	23,05 ↑	6,67	14,6	43,33	65	21,9	33,7	194 L
11	-	-	16,2	46	-	-	-	- '
12	9,2	4,35 1	10,7 L	36,641	84 ↑	24,7 ↑	29,3⊥	63 L
14	-		17,8	52		-	-	-
15	7,67	5,94	12,3	37,89	64	20,7	32,4	376
16	-	-	15,1	41	-	-	-	-
17	14,02	10,02 ↑	20,08 ↑	58,71 ↑	59 J	20,7	35,4↑	333
18	9,72	6,8	16,1	44,69	66	23,7	36,1 ↑	272
19	10,94	4,91↓	11,27 ↓	30,53↓	67	22,8	33,5	129 L
20	10,95	6,55	15,2	44,89	69	23,2	33,8	234
22	-	-	15,5	44		-	-	-
24	-	-	14,6	43	-	-	-	-
25	11,8	8,5	20,2 ↑	59,26 ↑	69,7	23,7	34,1 ↑	289
26	-	-	9,35↓	26 ↓		-	-	-
27	-	-	18,2 ↑	51		-	-	-
28	18,8	8,425	18,9 ↑	53	65	22,95	35,9 ↑	94 L
29	5,12↓	6,6	13,56	40	67	22,9	34,3 ↑	795 ↑
	7,92	5,81	14,7	36 ↓	62	25,3	40,9 ↑	-
30	-	-	15,6	48	-	-	-	-
32	19,72 ↑	3,67↓	9,2↓	26,22 ↓	67,9	25 ↑	36,7 ↑	114 L
33	13,385	2,38↓	5,55↓	14,91↓	68,3	25,6↑	37,45 ↑	59 ↓
34	-	-	8,3↓	26 ↓	-	-	-	-
36	-	-	17,7	45		-	-	-
38	21,09 ↑	3,77 ↓	9,85↓	28,49 1	61	22,6	37,1 ↑	338

Table 6. Biochemistry in dogs

Nr. case	BUN mg/d L	Creat. mg/dL	Glu mg/dL	Na mmol/L	K mmol/L	Total bilirubină mg/dL	Acidul lactic mmol/L
Normal	8-28	0,5-1,7	76-119	142-152	3,9-5,1	0,1-1,2	<2,5
6	7↓	0,9	97	144,9	4,14	12,1 ↑	
8	9	1,3	122 ↑	146,9	3,86↓	0,6	2,3
11	20	1,2	-	146,6	3,85↓	1,6↑	3,6 ↑
14	13	0,3↓	135 ↑	138,8↓	3,43↓	0,7	0,9
15	14	0,7	130 ↑	143,4	4,47	2,2 ↑	1,1
16	9,6	0,4↓	240 ↑	136 ↓	3,79↓	0,7	6,3↑
17	10	1,2	142 ↑	150,1	3,74 ↓	0,5	2,6 ↑
19	40 ↑	0,7	350 ↑	130,6↓	3,21↓	-	9,2 ↑
22	13	0,8	110	145,3	3,93	0,5	4,1↑
24	21	1,2	149 ↑	146,3	3,98	0,7	1,8
26	12,2	0,5	133,5 ↑	138,6 <u> </u>	4,21	3,7 ↑	2,8 ↑
27	9	1,2	128 ↑	141,8↓	3,87↓	0,7	2,3
28	16,5	1,1	121,66 ↑	147,5	4,35	4,5↑	3,65 ↑
29	12	1,1	123,33 ↑	144,2	4,04	3,5↑	2,36
30	29,5 ↑	2 ↑	97,5	149,6	3,9	1,8 ↑	1,5
32	34,5 ↑	2,8 ↑	260 ↑	125,5↓	5,16 ↑	-	15,5 ↑
34	12	1	-	142,7	3,82	5,2 ↑	1,9
36	14	1	131 ↑	146,1	3,97	0,6	2,2
37	19	1,2	76	148,1	4,6	-	3,7↑
38	-	0,5	150 †	137,9 L	4,32	0,5	2,7 †



Figure 1. Coagulogramma in dogs

CONCLUSIONS

In conclusion, out of 40 cases, 4 of them a cat and 3 dogs suffered simultaneously from kidney and liver diseases and if we take them individually, we had 2 cats and 3 dogs with kidney impairment and 2 cats and 8 dogs with liver disorders. Because we collected the data the archive of the Emergency from Veterinarian Hospital, our cases were accidental/intentional poisonings, we do not know the exact ingested dose, nor the time passed between the intoxication and the clinical examination, because of that we should take into account that the clinical signs, the laboratory data and paraclinical results can slightly differ depending on this and the individual response of the animal (breed, age, sex).

The recommendation for veterinarians is to make all possible examination of the patient as complete as possible, history, clinical examination, laboratory investigations and other paraclinical examinations show be done (echography, radiography) and prevention should be observed regarding to the protection of animals against this type of intoxication (Valchev et al., 2006).

A practicing clinician if at the clinical examination observe pale, anaemic mucous membranes, increases of the capillary refill time and external or internal bleeding, anticoagulant rodenticide poisoning should be put among the differential diagnose list. At the haematology part thrombocytopenia and low haemoglobin and haematocrit would be concerning, yet coagulogramma is the most trustful tulle to diagnose anticoagulant rodenticide intoxication, where we can see that the prothrombin time will increase and the partial activation thromboplastin time increase will be helpful in putting a positive diagnose.

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